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# The morphology, clinical significance and imaging methods of the atrial septal pouch: A critical review

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ABSTRACT

The purpose of this study was to present current knowledge about the atrial septal pouch, which is a relatively new anatomical discovery located within the human interatrial septum of the heart. The atrial septal pouch is formed during the postnatal partial fusion of the primary and secondary septum. The prevalence of the left septal pouch is 40.8%, the right septal pouch is present in 5.1% and a double pouch is seen in 3.7% of cases. The patent foramen ovale channel is present in 25.9% of all cases. The left septal pouch is a relatively small structure with an average depth of 8.4 ± 5.1 mm and mean volume of 0.31 ± 0.11 ml. The right septal pouch is significantly smaller than the left septal pouch, with a mean depth of 6.2 ± 3.4 mm and mean volume of 0.25 ± 0.08 ml. Both transesophageal echocardiography and cardiac computed tomography are useful techniques for detecting left septal pouches with the insignificant lower prevalence of detecting left septal pouches compared to the matched postmortem material. Transesophageal echocardiography with contrast modality seems to be superior than computed tomography due to its unambiguous patent foramen ovale channel detection and it should be the preferred imaging technique in clinical identification of septal pouches. The anatomy of left septal pouch may promote blood stasis and thrombus formation. Case reports and cross-sectional, single-center studies show that there is an association between the presence of a left sided septal pouch and an increased risk for cryptogenic stroke. Moreover, the left septal pouch may be an arrhythmogenic substrate responsible for triggering atrial fibrillation. The right septal pouch seems to have no clinical significance. In summary, the left septal pouch is the most common structure found within the interatrial septum and should be considered as a normal variant of the human heart anatomy. The morphological nature of the atrial septal pouch is well known, however, more clinical research is needed to resolve its possible connection with atrial fibrillation and cardio-embolic stroke.

## 1. Introduction

Up until recently, the interatrial septum of healthy individuals had two known basic anatomical variants: it existed as a smooth septum or a patent foramen ovale (PFO) channel [1]. In 2006, Breithardt et al. described a clinical case of a 25-year-old woman with a coronary artery embolus originating from a cavity of the interatrial septum [2]. Three years later, Krishnan and Salazar examined 94 randomly selected autopsied hearts and described a new anatomical entity – a blind ended pocket or diverticulum located within the human interatrial septum. They called it the atrial septal pouch, and it was present in 60% of their specimens [3]. This triggered an avalanche of research focusing on the morphology of the interatrial septum, and discussion began over the potential clinical significance of this small, newly uncovered structure [4–7]. In this critical review, we discuss the current state of knowledge about the atrial septal pouch, its etiology, morphology, clinical significance and imaging methods.

## 2. Etiology of the atrial septal pouches

The prenatal development of interatrial septation is well understood [1,8]. During the embryological period, the interatrial septum is not completely sealed, allowing direct blood flow from the right to left atrium (thereby omitting the pulmonary circulation). Just after birth, this connection closes naturally (functional closure), since increased blood pressure from the left atrium pushes the flap valve of the oval foramen (primary septum) against the so called “secondary septum”, which in fact is a deep infolding of the atrial wall [9]. According to the theory of lifelong remodeling of the human interatrial septum, constant friction between its subcomponents leads to micro-injuries and

*Abbreviations:* PFO, patent foramen ovale

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cicatrization of adjacent structures and ultimately, to the gradual closure of the connection [6]. In about one quarter of adults, this fusion does not occur, and there is a possible shunt between the atria thorough the PFO channel [6,7]. Meanwhile, partial fusion of the primary and secondary septum leads to the formation of the septal pouch. A long flap valve may fuse with the secondary septum at three levels. Fusion limited to the caudal portion of the zone of overlap leads to the creation of a left septal pouch, fusion limited to the central portion leads to a double septal pouch and fusion limited to the cranial portion forms a right septal pouch [3,6]. Further adhesion, especially of small pouches, results in the closure of the septal pouch and formation of a smooth septum in the elderly. In individuals with a short flap valve in the oval foramen (short PFO channel), fusion is complete and it results in full channel closure and a smooth septum at an early age [6]. It should be stressed that the PFO cannot co-exist with septal pouches, which is a common mistake made by those unfamiliar with the theory of septal pouch formation.

## 3. Morphology of the atrial septal pouches

The atrial septal pouch is a kangaroo-like pocket located on either the right, left or both sides of the interatrial septum. When the septal pouch is present, there is no observed connection which joins the atria. A cadaveric study performed on a total of 294 healthy adult hearts showed the presence of a left septal pouch in 40.8% of cases. The right septal pouch was present in 5.1% whereas a double pouch was observed is 3.7%. The PFO channel was found in 25.9% of all cases [3,6]. A study by Hołda et al. found that the PFO was more prevalent in younger people. Conversely, septal pouches and smooth septums were more frequent in older individuals, further supporting the theory of lifelong interatrial septum remodeling [6]. The results presented above clearly show that the left septal pouch is the most common structure seen within the interatrial septum, and it should be considered a normal variant of the human heart anatomy.

The left septal pouch (Fig. 1) is located at the junction of the anterior wall of left atrium and the left side of the interatrial septum. The left septal pouch is composed of a free wall (remnant of the PFO channel flap valve), an atrial wall, an ostium, an apex and a lumen. Its apex is oriented downwards, and its ostium is positioned at an angle of 10–50° to the left [6]. A webbed (or net-like) structure may sometimes be observed in the ostium of the left septal pouch [10]. The contour of

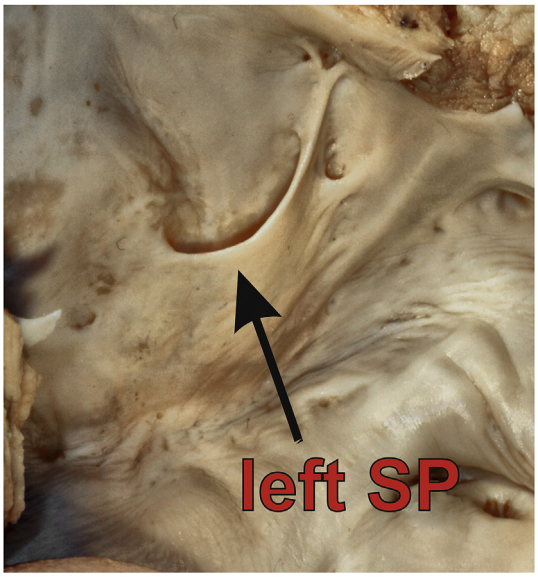


**Fig. 1.** Photograph showing cadaveric heart specimens. Intracavitary view of the left side of interatrial septum showing left septal pouch (SP).

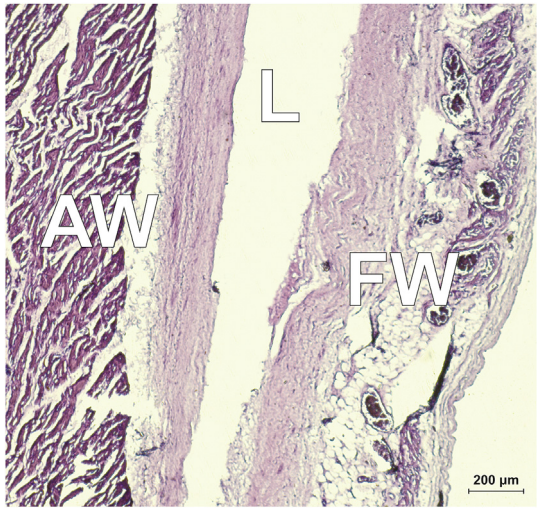


**Fig. 2.** Histological section of the left septal pouch (hematoxylin and eosin staining). Layers from the left atrium cavity (free wall – FW): endocardium, transverse muscle fibers, connective tissue, endocardium, septal pouch lumen (L), atrial endocardium, subendocardial connective tissue, deep atrial muscle fibers (atrial wall – AW).

the left septal pouch is projected onto the transverse pericardial sinus and then onto the non-coronary sinus of the aortic valve. Moreover, the left septal pouch does not overlap with any of the true interatrial septum components [6,7]. Casts of autopsied hearts (made with acrylic mass), showed that the left septal pouch has a conical or cylindrical shape, with some smaller diverticula originating from its main body [6]. The depth of the left septal pouch (measured from the ostium to the apex) is estimated to be about 8.4 ± 5.1 mm and its mean volume is 0.31 ± 0.11 ml. When comparing the volume of the left atrial appendage to the volume of the left septal pouch, we see that the latter makes up only 13.6 ± 9.4% (range: 3.1–44.9%) of the appendage [6]. Hence, the left septal pouch is a relatively small structure. Using routine hematoxylin-eosin histological staining, the microscopic morphology of the left septal pouch was examined as well (Fig. 2). It showed that the free wall of the septal pouch is composed of two distinct layers of endocardium, separated by transverse muscle fibers and connective tissue. The atrial wall of the left septal pouch is morphologically typical of an atrium with rich muscle layer covered by endocardium. The presence of muscular tissue may allow contractions and emptying blood out of the lumen of the septal pouch. In the apex of the septal pouch, there is an accumulation of sub-endocardial connective tissue, which supports the theory of a fusing PFO channel and further development into a septal pouch [6].

The construction and orientation of the right septal pouch is different. The right septal pouch is bounded from the right side by the antero-superior rim of the fossa ovalis and from the left side by the fossa ovalis floor. Its apex is directed upwards, and the ostium is directed towards the inferior vena cava [6]. The orifice of the right septal pouch is predominantly located in the supero-anterior circumference of the fossa ovalis (62.5%); in 25.0% it is located in the supero-central, in 6.25% in supero-posterior and in 6.25% in the anterior circumference of the oval fossa [7]. The right septal pouch is significantly smaller than the left septal pouch, having an average mean depth of 6.2 ± 3.4 mm and a mean volume of 0.25 ± 0.08 ml [6].

## 4. Medical imaging of the septal pouches

The atrial septal pouch can be visualized *in vivo* using several imaging techniques. Transesophageal echocardiography is the best approach for imaging the interatrial septum region, which is poorly seen in transthoracic echocardiography due to its posterior position in

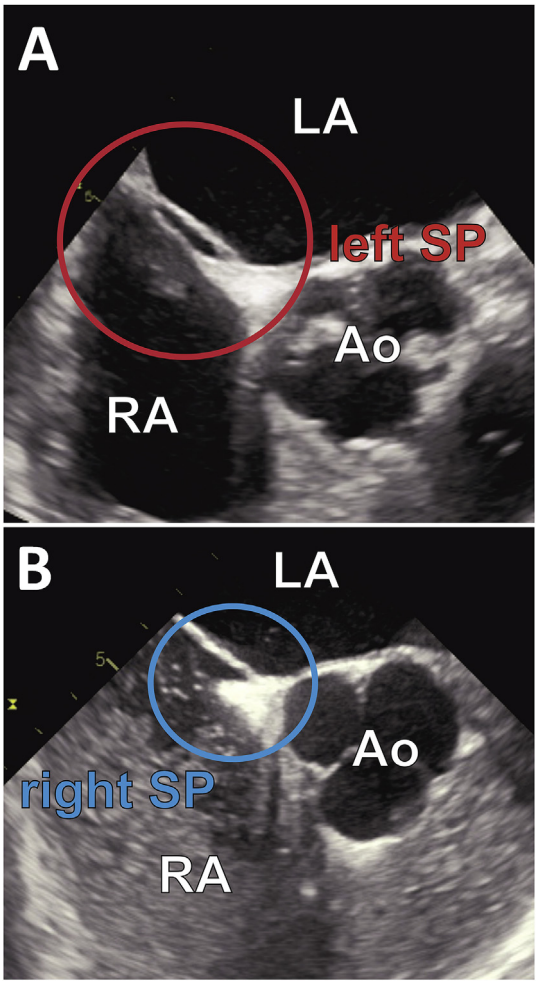


**Fig. 3.** Transesophageal echocardiography view of the (A) left septal pouch and (B) right septal pouch.
AO - Aorta; LA - left atrium; RA - right atrium; SP - septal pouch.

relation to other structures of the heart and chest [11]. Transesophageal echocardiography with agitated saline injection along with the Valsalva maneuver seem to be the golden standard for atrial septal pouch visualization (Fig. 3) [12,13]. The saline contrast injection detects the presence of the PFO channel, thereby excluding the possibility of an existing septal pouch [14]. Two transesophageal echocardiography projections are commonly used for interatrial septum visualization: mid-esophageal bicaval view and mid-esophageal short-axis view [15]. A technically oriented study performed by Hołda et al. concluded that evidence of a septal pouch should be confirmed by a minimum of two different views. Regardless, the bicaval view has been shown to provide a superior anatomical view of the left septal pouch, since it gives a projection of the interatrial septum that is oriented along the same line as the long-axis of the pouch. Therefore, the mid-esophageal bicaval view should be the preferred approach when viewing and measuring the left septal pouch [12]. A comparison of clinical imaging using the transesophageal echocardiography with the sex-, age- and BMI-matched autopsied hearts found that the prevalence of the left septal pouch was lower when evaluated by echocardiography than by anatomical dissection, but this difference was found to be statistically insignificant (39.3% vs. 44.0%, p = 0.56). The same conclusions were observed for the right (echo: 11.3% vs. autopsy: 14.0%, p = 0.61) and for the double septal pouch (echo: 4.7% vs. autopsy: 6.0%, p = 0.71). Transesophageal echocardiography measurements of both left and right septal pouches yielded significantly smaller measurements when compared to cadaveric material [13]. In their study, Elsayed et al. found that the 3D

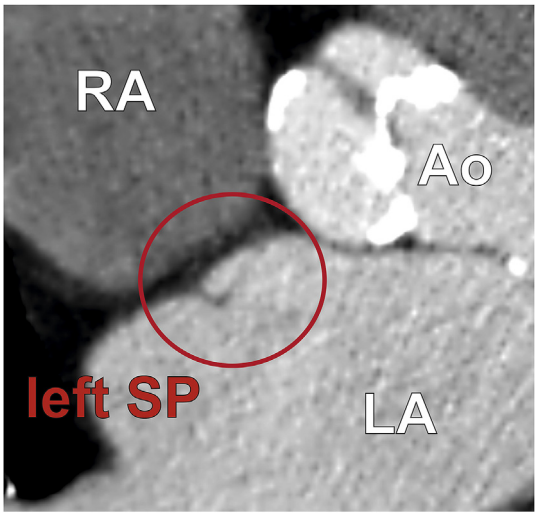


**Fig. 4.** Contrast enhanced ECG-gated cardiac multidetector row computed tomography view of the left septal pouch.
AO - Aorta; LA - left atrium; RA - right atrium; SP - septal pouch.

transesophageal echocardiography was superior to 2D imaging in the number of perceived septal pouches. When available, 3D techniques should also be used to detect these structures [16,17].

Contrast enhanced ECG-gated cardiac multidetector row computed tomography seems to also be a valuable tool for clinical imaging of the interatrial septum (Fig. 4) [18,19]. However, cardiac computed tomography was shown to be less precise at identifying septal pouches than transesophageal echocardiography. The main shortcoming of this technique is associated with its inability to properly detect the PFO channel, whose flap valve may be confused with the left septal pouch. Moreover, the computed tomography should not be used for detection and evaluation of right septal pouches, since low blood contrast in the right atrium significantly hinders the evaluation of right-sided interatrial septum structures [13].

The septal pouch is also visible in cardiac magnetic resonance imaging, but so far no study has investigated the accuracy and usefulness of this imaging method in the detection and assessment of atrial septal pouches [2].

## 5. Clinical significance of the septal pouches

Is the atrial septal pouch just an anatomical variation of the interatrial septum, or does it have some clinical importance? Many researchers have pondered this difficult question, from the moment of its discovery [3]. The first clinical cases involving the left septal pouch have linked its presence to ischemic stroke and showed thrombi originating from the interior of its pouch [20–27]. Unfortunately, based on the preliminary epidemiologic retrospective studies, the association between the presence of a left septal pouch and an increased risk of cryptogenic stroke was controversial [28–33]. A meta-analysis performed in 2017 by Strachinaru et al. detected no difference in left septal pouch prevalence between non-stroke controls and patients with ischemic stroke (both cryptogenic and with a known cause) (HR = 1.20; 95%Cl = 0.96–1.53; p = 0.14). However, cryptogenic stroke was shown to be more frequent in patients with a left septal pouch (HR = 1.53; 95%Cl = 1.07–2.24; p = 0.02) [34]. Lastly, a study by Hołda et al. on 126 patients with cryptogenic stroke and 137 age-matched controls without stroke showed that the presence of a left septal pouch was associated with an increased risk for cryptogenic stroke (OR = 2.02; 95% CI: 1.19–3.41; p = 0.01).

It should be highlighted that the mechanism behind the left septal pouch involvement in stroke is different than that of a PFO channel. The PFO channel is responsible for ischemic stroke through a paradoxical

embolism mechanism which will not be present in patients with a left septal pouch, because there is no connection between both atria in such a variation. Instead of this, local thrombosis within the atrial septal pouch is thought to be the main pathophysiological mechanism [35]. The anatomy of the left septal pouch may be responsible for blood stasis and thrombus formation (a calyx covered with endocardium and filled with blood) [6]. A brisk laminar blood flow from the right pulmonary veins is considered to be a protective mechanism against clot formation within the left septal pouch lumen [24]. Any disturbances to the blood flow as well as conditions leading to peri-wall atrial blood stasis (high ventricular pressure, mitral stenosis, heart failure, and atrial fibrillation) may be prothrombogenic [6,35,36]. The presence of a left septal pouch may also be associated with unexplained transient ischemic attacks which occur after *trans*-septal puncture, since the needle may enable the release of embolic material from the lumen of the left septal pouch [6].

Moreover, the presence of a left-sided septal pouch is associated with a higher prevalence of atrial fibrillation. The explanation about why the left septal pouch may trigger arrythmias is rooted in its etiology (fusion of PFO channel) and may also be related to the presence of scar tissue in the septal pouch apex, which may be proarrhythmogenic [19].

Yilmaz et al. have linked migraine etiology and interatrial septum conformation. They noticed that the presence of an atrial septal pouch may be a prominent risk factor for distal embolization, observed in patients with migraines with aura [37]. However, more studies in this area are needed to confirm this association.

Lastly, to our knowledge, the right septal pouch seems to have no clinical significance.

## 6. Atrial septal pouches in other species

There may possibly be a need to learn about management strategies associated with septal pouches. Any new devices or trials should first be tested on animals, so it seems rational to search septal pouches in other species. Unfortunately, to date, the presence of a left atrial septal pouch has only been described in humans. In their study, Hołda et al. examined 75 interatrial septa of swine hearts. No left or double atrial septal pouches were found, although the right septal pouch was detected in 22.7% of hearts and the PFO channel was also present in 22.7% of specimens. Instead of a left septal pouch, the left septal ridge (a tissue fold on the left side of the interatrial septum) was found in one quarter of cases [38]. Interspecies differences pertaining to the structure of the interatrial septum may be explained by several factors, including the unguligrade posture of swine, a different arrangement of caval veins (inferior vena cava rotation toward the left side) and a different arrangement and number of pulmonary veins which could shorten the PFO channel [38–41]. The absence of a left septal pouch in swine demonstrates that the porcine heart is an unsuitable experimental model for left septal pouch management.

## 7. Conclusions

The morphological nature of the atrial septal pouch is well known; however more research is needed to resolve its clinical significance. A better understanding and awareness of this structure, especially the left-sided one, may revolutionize the area of cardiac-related stroke, as this structure may be one of the contributors of thrombus formation within the left atrium. The recent discovery of the atrial septal pouch is a beautiful reminder that not everything is known about human gross anatomy. Morphological studies may lead to more breakthroughs, with potential implications on daily clinical practice.

## Conflicts of interest

The authors declare that they have no conflict of interest.

## Ethical statement

No humans or animals were part of this study. All authors contributed to and approved this manuscript.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tria.2018.11.002.

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